STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 106282

TO:	From :
Lawrence E Crane Location: CM-1/8D14/8B19 Art Unit : 1623 Thursday, October 30, 2003 Case Serial Number: 09/363748	Susan Hanley Location: Biotech-Chem Library CM1 6B05 Phone: 305-4053 susan.hanley@uspto.gov

Search Notes

Access DB# 106282

Search Request Form

Scientific and Technical Information Center

Requester's Full Name: L. Eric Crane Examiner #: 65753 Date: **10/20/03**
Art Unit: 1623 Phone Number: **308-4639** Serial No. **09/363,748.**
Mail Box & Bldg/Room Loc: 8D-14/CM-1 Results Format Preferred: **PAPER [8B-19/CM-1]**

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, key words, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known. Please attach a copy of the cover sheet, pertinent claims, and/or abstract..

Title of Invention: See attached copy of claims.
Inventors (please provide full names): See attached copy of claims.
Earliest Priority Filing Date: **07/31/98**

**For Sequence Searches only* Please include all of the pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search for the administration of "a uridine phosphate" (Uridine monophosphate, -diphosphate, -triphosphate, -tetraphosphate, etc. aka UMP, UDP, UTP, etc..) to enhance memory in a host in need thereof. Please also search for a first additional ingredient from the lists found in claims 46, 47 and 48 and a second additional ingredient from the list in claim 49.

RECEIVED OCT 20 2003 TECH CENTER

4/

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STAFF USE ONLY

	Type of Search	Vendors/cost as applicable
Searcher: Hurley	NA Sequence(#) _____	STN _____
Searcher Phone #: _____	AA Sequence(#) _____	Dialog _____
Searcher Location: _____	Structure (#) _____	Questel/Orbit _____
Date Searcher Picked Up: 10/23	Bibliographic _____	Dr. Link _____
Date Completed: _____	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: _____	Full Text _____	Seq.Syst'ms _____
Clerical Prep Time: _____	Patent Family _____	WWW/Internet _____
Online Time: _____	Other _____	Other(Specify) _____

RECEIVED OCT 20 2003 STIC

PTO-1590 (8-2001)

pt 1 of 2

```
=> file medline
FILE 'MEDLINE' ENTERED AT 18:21:62 ON 30 OCT 2003

 FILE LAST UPDATED: 29 OCT 2003 (20031029/UP).  FILE COVERS 1958 TO DATE.

 On April 13, 2003, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary.  See http://www.nlm.nih.gov/mesh/changes2003.html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
```

CT= controlled terms
NT = narrower term

```
=> d que l49

L1         3391 SEA FILE=REGISTRY ABB=ON  PLU=ON  "URIDINE" AND "PHOSPHATE"
L2         1177 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 AND NRS=2
L42        2979 SEA FILE=MEDLINE ABB=ON  PLU=ON  L2
L44       45374 SEA FILE=MEDLINE ABB=ON  PLU=ON  MEMORY+NT/CT
L49           2 SEA FILE=MEDLINE ABB=ON  PLU=ON  L42 AND L44


=> d que l51

L1         3391 SEA FILE=REGISTRY ABB=ON  PLU=ON  "URIDINE" AND "PHOSPHATE"
L2         1177 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 AND NRS=2
L42        2979 SEA FILE=MEDLINE ABB=ON  PLU=ON  L2
L47       10720 SEA FILE=MEDLINE ABB=ON  PLU=ON  MEMORY DISORDERS+NT/CT
L48       30476 SEA FILE=MEDLINE ABB=ON  PLU=ON  ALZHEIMER DISEASE/CT
L51           0 SEA FILE=MEDLINE ABB=ON  PLU=ON  L42 AND (L47 OR L48)
```

TU= therapeutic
AD= admin & dosage
PK= pharmacokinetics
PD= Pharmacology
AE= adverse effect

```
=> d que l56

L44       45374 SEA FILE=MEDLINE ABB=ON  PLU=ON  MEMORY+NT/CT
L45       24791 SEA FILE=MEDLINE ABB=ON  PLU=ON  URIDINE+NT/CT
L46        9733 SEA FILE=MEDLINE ABB=ON  PLU=ON  URACIL NUCLEOTIDES+NT/CT
L47       10720 SEA FILE=MEDLINE ABB=ON  PLU=ON  MEMORY DISORDERS+NT/CT
L48       30476 SEA FILE=MEDLINE ABB=ON  PLU=ON  ALZHEIMER DISEASE/CT
L53       10243 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L45 OR L46)(L)(TU OR AD OR
                 PK OR PD OR AE)/CT
L54          12 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L44 OR (L47 OR L48)) AND L53

L55          11 SEA FILE=MEDLINE ABB=ON  PLU=ON  L54 AND (MEMORY OR LEARN?)
L56           4 SEA FILE=MEDLINE ABB=ON  PLU=ON  L55 AND ?PHOSPHATE


=> s l49 or l51 or l56

L94           5 L49 OR L51 OR L56
```

5 cites from medline

```
=> file drugu

FILE 'DRUGU' ENTERED AT 18:21:05 ON 30 OCT 2003
COPYRIGHT (C) 2003 THOMSON DERWENT

FILE LAST UPDATED: 23 OCT 2003       <20031023/UP>
>>>  DERWENT DRUG FILE (SUBSCRIBER)  <<<

>>>  SDI'S MAY BE RUN WEEKLY OR MONTHLY AS OF JUNE 2001.  <<<
>>>  (WEEKLY IS THE DEFAULT). FOR PRICING INFORMATION     <<<
>>>  SEE HELP COST                                        <<<

>>>  FILE COVERS 1983 TO DATE  <<<
>>>  THESAURUS AVAILABLE IN /CT  <<<
```

```
=> d que l65

L63         269 SEA FILE=DRUGU ABB=ON  PLU=ON  (URIDIN? OR URACIL)(5A)(PHOSPHAT
                E OR MONOPHOSPH? OR DIPHOSPH? OR TRIPHOSPH?)
L64       13997 SEA FILE=DRUGU ABB=ON  PLU=ON  MEMORY OR LEARNING OR COGNIT?
                OR AMNESI?
L65           0 SEA FILE=DRUGU ABB=ON  PLU=ON  L63 AND L64
```

no cites from drugu

```
=> file embase

FILE 'EMBASE' ENTERED AT 18:21:07 ON 30 OCT 2003
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 FILE COVERS 1974 TO 30 Oct 2003 (20031030/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que l74

L66      169222 SEA FILE=EMBASE ABB=ON  PLU=ON  MEMORY OR LEARNING OR COGNIT?
                OR AMNESI?
L67        7755 SEA FILE=EMBASE ABB=ON  PLU=ON  (URIDIN? OR URACIL)(5A)(PHOSPHA
                TE OR MONOPHOSPH? OR DIPHOSPH? OR TRIPHOSPH?)
L68          22 SEA FILE=EMBASE ABB=ON  PLU=ON  L66 AND L67
L69         645 SEA FILE=EMBASE ABB=ON  PLU=ON  URIDINE PHOSPHATE/CT
L70         729 SEA FILE=EMBASE ABB=ON  PLU=ON  URIDINE DIPHOSPHATE/CT
L71        2246 SEA FILE=EMBASE ABB=ON  PLU=ON  URIDINE TRIPHOSPHATE/CT
L73         390 SEA FILE=EMBASE ABB=ON  PLU=ON  (L69 OR L70 OR L71)(L)(PD OR
                DO OR DV OR TU)/CT
L74           3 SEA FILE=EMBASE ABB=ON  PLU=ON  L73 AND L68
```

PD = pharmacology
DO = dosage
DV = drug development
TU = therapy

```
=> d que l83

L66      169222 SEA FILE=EMBASE ABB=ON  PLU=ON  MEMORY OR LEARNING OR COGNIT?
                OR AMNESI?
L69         645 SEA FILE=EMBASE ABB=ON  PLU=ON  URIDINE PHOSPHATE/CT
L70         729 SEA FILE=EMBASE ABB=ON  PLU=ON  URIDINE DIPHOSPHATE/CT
L71        2246 SEA FILE=EMBASE ABB=ON  PLU=ON  URIDINE TRIPHOSPHATE/CT
L75        7418 SEA FILE=EMBASE ABB=ON  PLU=ON  CHOLINE/CT
L77        3272 SEA FILE=EMBASE ABB=ON  PLU=ON  SPHINGOMYELIN/CT
L78        6969 SEA FILE=EMBASE ABB=ON  PLU=ON  LECITHIN
L79        1111 SEA FILE=EMBASE ABB=ON  PLU=ON  LYSOLECITHIN
L81        4760 SEA FILE=EMBASE ABB=ON  PLU=ON  PHOSPHATIDYLETHANOLAMINE/CT
L82          48 SEA FILE=EMBASE ABB=ON  PLU=ON  L66 AND (L75 OR (L77 OR L78 OR
                L79) OR L81)(L)(TU OR PD OR DO OR DV OR DC)/CT
L83           1 SEA FILE=EMBASE ABB=ON  PLU=ON  L82 AND (L69 OR L70 OR L71)
```

DC = drug comparison

```
=> d que l89

L66      169222 SEA FILE=EMBASE ABB=ON  PLU=ON  MEMORY OR LEARNING OR COGNIT?
                OR AMNESI?
L86         827 SEA FILE=EMBASE ABB=ON  PLU=ON  PHOSPHORYLASE(5A)INHIBIT?
L87         102 SEA FILE=EMBASE ABB=ON  PLU=ON  URIDINE(5A)(RENAL OR SECRET?
                OR COMPET?)
L88           2 SEA FILE=EMBASE ABB=ON  PLU=ON  (L86 OR L87) AND L66
L89           0 SEA FILE=EMBASE ABB=ON  PLU=ON  L88 AND (URIDINE OR URACIL)

=> s l74 or l83 or l89
```

L95 3 L74 OR L83 OR L89 3 cites for embase

=> file hcaplus

FILE 'HCAPLUS' ENTERED AT 18:21:09 ON 30 OCT 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 30 Oct 2003 VOL 139 ISS 18
FILE LAST UPDATED: 29 Oct 2003 (20031029/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> d que l14

L1 3391 SEA FILE=REGISTRY ABB=ON PLU=ON "URIDINE" AND "PHOSPHATE"
L2 1177 SEA FILE=REGISTRY ABB=ON PLU=ON L1 AND NRS=2
L3 10669 SEA FILE=HCAPLUS ABB=ON PLU=ON L2
L4 1095 SEA FILE=HCAPLUS ABB=ON PLU=ON L3(L)(THU OR PKT OR PAC OR DMA OR BAC)/RL
L9 1475 SEA FILE=HCAPLUS ABB=ON PLU=ON AMNESIA/CT
L10 30335 SEA FILE=HCAPLUS ABB=ON PLU=ON MENTAL ACTIVITY+PFT,NT/CT
L14 2 SEA FILE=HCAPLUS ABB=ON PLU=ON (L9 OR L10) AND L4

PFT = old, new or "used for" terms
THU = therapy
PKT = pharmacokinetics
PAC = pharmacol.
DMA = drug mech of action
BAC = Biol. action

=> d que l21

L1 3391 SEA FILE=REGISTRY ABB=ON PLU=ON "URIDINE" AND "PHOSPHATE"
L2 1177 SEA FILE=REGISTRY ABB=ON PLU=ON L1 AND NRS=2
L9 1475 SEA FILE=HCAPLUS ABB=ON PLU=ON AMNESIA/CT
L10 30335 SEA FILE=HCAPLUS ABB=ON PLU=ON MENTAL ACTIVITY+PFT,NT/CT
L15 20 SEA FILE=HCAPLUS ABB=ON PLU=ON L2 AND (L9 OR L10)
L21 11 SEA FILE=HCAPLUS ABB=ON PLU=ON L15 AND MEMORY

=> d que l23

L1 3391 SEA FILE=REGISTRY ABB=ON PLU=ON "URIDINE" AND "PHOSPHATE"
L2 1177 SEA FILE=REGISTRY ABB=ON PLU=ON L1 AND NRS=2 # ring systems = NRS
L3 10669 SEA FILE=HCAPLUS ABB=ON PLU=ON L2
L4 1095 SEA FILE=HCAPLUS ABB=ON PLU=ON L3(L)(THU OR PKT OR PAC OR DMA OR BAC)/RL
L11 2285 SEA FILE=HCAPLUS ABB=ON PLU=ON COGNITION ENHANCERS+PFT/CT
L12 3634 SEA FILE=HCAPLUS ABB=ON PLU=ON "ANTI-ALZHEIMER'S AGENTS"/CT
L23 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L4 AND (L11 OR L12)

=> d que l29

L5 1184 SEA FILE=HCAPLUS ABB=ON PLU=ON PYRIMIDINE NUCLEOSIDES+PFT/CT

L7 1057 SEA FILE=HCAPLUS ABB=ON PLU=ON PYRIMIDINE NUCLEOTIDES+PFT/CT

```
L9          1475 SEA FILE=HCAPLUS ABB=ON  PLU=ON  AMNESIA/CT
L10        30335 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MENTAL ACTIVITY+PFT,NT/CT
L27            5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L5 OR L7) AND (L9 OR L10)
L28            4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L27 AND (?URIDIN? OR ?URACIL?)

L29            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28 NOT (METHYLGLUCAMINE)/TI


=> d que l35

L1          3391 SEA FILE=REGISTRY ABB=ON  PLU=ON  "URIDINE" AND "PHOSPHATE"
L2          1177 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 AND NRS=2
L3         10669 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2
L9          1475 SEA FILE=HCAPLUS ABB=ON  PLU=ON  AMNESIA/CT
L10        30335 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MENTAL ACTIVITY+PFT,NT/CT
L11         2285 SEA FILE=HCAPLUS ABB=ON  PLU=ON  COGNITION ENHANCERS+PFT/CT
L12         3634 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "ANTI-ALZHEIMER'S AGENTS"/CT
L13        44995 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PHOSPHATIDYLCHOLINES+PFT,NT/CT

L34           91 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 AND (L9 OR L10 OR L11 OR
                 L12)
L35            0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L34 AND L3


=> d que l36

L5          1184 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PYRIMIDINE NUCLEOSIDES+PFT/CT

L7          1057 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PYRIMIDINE NUCLEOTIDES+PFT/CT

L9          1475 SEA FILE=HCAPLUS ABB=ON  PLU=ON  AMNESIA/CT
L10        30335 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MENTAL ACTIVITY+PFT,NT/CT
L11         2285 SEA FILE=HCAPLUS ABB=ON  PLU=ON  COGNITION ENHANCERS+PFT/CT
L12         3634 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "ANTI-ALZHEIMER'S AGENTS"/CT
L13        44995 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PHOSPHATIDYLCHOLINES+PFT,NT/CT

L34           91 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 AND (L9 OR L10 OR L11 OR
                 L12)
L36            0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L34 AND (L5 OR L7)


=> d que l37

L9          1475 SEA FILE=HCAPLUS ABB=ON  PLU=ON  AMNESIA/CT
L10        30335 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MENTAL ACTIVITY+PFT,NT/CT
L11         2285 SEA FILE=HCAPLUS ABB=ON  PLU=ON  COGNITION ENHANCERS+PFT/CT
L12         3634 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "ANTI-ALZHEIMER'S AGENTS"/CT
L13        44995 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PHOSPHATIDYLCHOLINES+PFT,NT/CT

L34           91 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 AND (L9 OR L10 OR L11 OR
                 L12)
L37            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L34 AND (?URIDIN? OR ?URACIL?)


=> s l14 or l21 or l23 or l29 or l35-37

L96           18 L14 OR L21 OR L23 OR L29 OR (L35 OR L36 OR L37)  18 cites for HCAPLUS

=> dup rem l94 l65 l95 l96   removing duplicate cites
L65 HAS NO ANSWERS
FILE 'MEDLINE' ENTERED AT 18:21:52 ON 30 OCT 2003

FILE 'EMBASE' ENTERED AT 18:21:52 ON 30 OCT 2003
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FILE 'HCAPLUS' ENTERED AT 18:21:52 ON 30 OCT 2003
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PROCESSING COMPLETED FOR L94
PROCESSING COMPLETED FOR L65
PROCESSING COMPLETED FOR L95
PROCESSING COMPLETED FOR L96
L97 24 DUP REM L94 L65 L95 L96 (2 DUPLICATES REMOVED) 24 cites
ANSWERS '1-5' FROM FILE MEDLINE
ANSWERS '6-8' FROM FILE EMBASE
ANSWERS '9-24' FROM FILE HCAPLUS

=> d ibib abs ind 1

L97 ANSWER 1 OF 24 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 78245511 MEDLINE
DOCUMENT NUMBER: 78245511 PubMed ID: 682696
TITLE: Retention improvement by topical application of uridine **monophosphate** into different brain areas.
AUTHOR: Ott T; Grecksch G; Matthies H
SOURCE: MEDICAL BIOLOGY, (1978 Jun) 56 (3) 133-7.
Journal code: 0417300. ISSN: 0302-2137.
PUB. COUNTRY: Finland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197810
ENTRY DATE: Entered STN: 19900314
Last Updated on STN: 19970203
Entered Medline: 19781027

AB This study aimed to demonstrate the effect of uridine **monophosphate** (UMP) on the consolidation of a brightness-discrimination reaction after topical application of this RNA precursor into the hippocampus, the neocortex or the mesencephalic reticular formation (MRF). Thirty minutes before the rats started their training in a Y-chamber, UMP was injected into each animal through cannula implanted into the particular brain area. When injected into hippocampus or MRF UMP exerted no influence on acquisition, but after epidural UMP injection an impairment of acquisition was observed. After intrahippocampal or epidural UMP application the retention test carried out 48 hour after training showed a significant improvement in retention performance, whereas UMP injection into MRF showed no influence on retention. Consequently, the retention-improving effect of UMP is probably not induced by activation of ascending neuronal systems.

CT Check Tags: Animal; Comparative Study; Male
Administration, Topical
Behavior, Animal: DE, drug effects
*Brain: DE, drug effects
Cerebral Cortex: DE, drug effects
Conditioning (Psychology): DE, drug effects
Hippocampus: DE, drug effects
Learning: DE, drug effects
***Memory: DE, drug effects**
Mesencephalon: DE, drug effects
Rats
***Retention (Psychology): DE, drug effects**
Reticular Formation: DE, drug effects
***Uracil Nucleotides: PD, pharmacology**
Uridine Monophosphate: AD, administration & dosage
***Uridine Monophosphate: PD, pharmacology**
RN **58-97-9 (Uridine Monophosphate)**
CN 0 (Uracil Nucleotides)

=> d ibib abs ind 2-5

L97 ANSWER 2 OF 24 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 73207466 MEDLINE
DOCUMENT NUMBER: 73207466 PubMed ID: 4714676
TITLE: Suppression of uridine **monophosphate**-induced improvement in long-term storage by cycloheximide.
AUTHOR: Ott T; Matthies H
SOURCE: PSYCHOPHARMACOLOGIA, (1973) 28 (1) 103-6.
Journal code: 7609417. ISSN: 0033-3158.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197308
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19730831

CT Check Tags: Animal
Conditioning (Psychology)
Cycloheximide: PD, pharmacology
Drug Antagonism
Escape Reaction
***Memory: DE, drug effects**
Proteins: BI, biosynthesis
RNA: BI, biosynthesis
Rats
Time Factors
***Uracil Nucleotides: PD, pharmacology**
RN 63231-63-0 (RNA); 66-81-9 (Cycloheximide)
CN 0 (Proteins); 0 (Uracil Nucleotides)

L97 ANSWER 3 OF 24 MEDLINE on STN
ACCESSION NUMBER: 97198255 MEDLINE
DOCUMENT NUMBER: 97198255 PubMed ID: 9046309
TITLE: Improvement of cognitive deficits and decreased cholinergic neuronal cell loss and apoptotic cell death following neurotrophin infusion after experimental traumatic brain injury.
AUTHOR: Sinson G; Perri B R; Trojanowski J Q; Flamm E S; McIntosh T K
CORPORATE SOURCE: Division of Neurosurgery, University of Pennsylvania School of Medicine, Philadelphia, USA.
CONTRACT NUMBER: GM34690 (NIGMS)
NS P01-08803 (NINDS)
NS R01-26818 (NINDS)
SOURCE: JOURNAL OF NEUROSURGERY, (1997 Mar) 86 (3) 511-8.
Journal code: 0253357. ISSN: 0022-3085.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970407
Last Updated on STN: 19980206
Entered Medline: 19970324

AB This study explores the effects of infusion of nerve growth factor (NGF) on behavioral outcome and cell death in the septal region using the clinically relevant model of fluid-percussion brain injury in the rat. Animals were subjected to fluid-percussion brain injury and 24 hours later a miniosmotic pump was implanted to infuse NGF (12 animals) or vehicle (12 animals) directly into the region of maximum injury for 2 weeks. Four weeks postinjury the animals were tested for cognitive function using a Morris Water Maze paradigm. Neurological motor function was evaluated over a 4-week postinjury period. The rats receiving NGF infusions had significantly higher memory scores than vehicle-treated animals. Examination of the cholinergic neurons in the medial septal region using choline acetyltransferase immunohistochemistry demonstrated significant cell loss after injury. Infusion of NGF significantly attenuated loss of these cholinergic neurons. A second group of animals was subjected to

fluid-percussion brain injury alone (23 rats) or injury followed by NGF infusion (18 rats). These animals were killed between 24 hours and 2 weeks postinjury and the septal region was examined for the presence of apoptotic cells using the terminal deoxynucleotidyl transferase-mediated biotinylated-deoxyuridinetriphosphate nick-end labeling technique. Apoptotic cells were identified as early as 24 hours postinjury; their numbers peaked at 4 and 7 days, and then declined by 14 days. The NGF-treated animals had some apoptotic cells; however, even at 7 days there were significantly fewer of these cells. No significant motor differences were observed between the NGF- and vehicle-treated groups. These data indicate that NGF administration beginning 24 hours after fluid-percussion brain injury has a beneficial effect on cognition and results in sparing of cholinergic septal neurons. These improvements persist after cessation of NGF administration. The beneficial effects of NGF may be related to its ability to attenuate traumatically induced apoptotic cell death.

CT Check Tags: Animal; Male; Support, U.S. Gov't, P.H.S.
Apoptosis: DE, drug effects
Behavior, Animal: DE, drug effects
*Brain Injuries: DT, drug therapy
Brain Injuries: PA, pathology
Cell Count
Cell Death: DE, drug effects
Choline O-Acetyltransferase: DU, diagnostic use
*Cholinergic Fibers: DE, drug effects
Cholinergic Fibers: PA, pathology
Cognition: DE, drug effects
*Cognition Disorders: DT, drug therapy
DNA Nucleotidylexotransferase: DU, diagnostic use
Deoxyuracil Nucleotides: DU, diagnostic use
Hippocampus: DE, drug effects
Hippocampus: IN, injuries
Hippocampus: PA, pathology
Infusion Pumps
Memory: DE, drug effects
Motor Neurons: DE, drug effects
Nerve Growth Factors: AD, administration & dosage
*Nerve Growth Factors: TU, therapeutic use
*Neurons: DE, drug effects
Neurons: PA, pathology
Parietal Lobe: DE, drug effects
Parietal Lobe: IN, injuries
Parietal Lobe: PA, pathology
Psychomotor Performance: DE, drug effects
Rats
Rats, Sprague-Dawley
Septal Nuclei: DE, drug effects
Septal Nuclei: IN, injuries
Septal Nuclei: PA, pathology
Time Factors
Vehicles

RN **1173-82-6 (deoxyuridine triphosphate)**

CN 0 (Deoxyuracil Nucleotides); 0 (Nerve Growth Factors); 0 (Vehicles); EC 2.3.1.6 (Choline O-Acetyltransferase); EC 2.7.7.31 (DNA Nucleotidylexotransferase)

L97 ANSWER 4 OF 24 MEDLINE on STN
ACCESSION NUMBER: 74127786 MEDLINE
DOCUMENT NUMBER: 74127786 PubMed ID: 4817915
TITLE: Increase of guanosine incorporation into RNA of hippocampal neurons by application of uridine **monophosphate** during a **learning** experiment.
AUTHOR: ~~Ruthrich H L; Pohle W; Matthies H~~
SOURCE: BRAIN RESEARCH, (1974 Mar 29) 69 (1) 49-55.
Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197405
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19740528
CT Check Tags: Animal
Autoradiography
Behavior, Animal: DE, drug effects
Discrimination Learning: DE, drug effects
*Guanosine: ME, metabolism
*Hippocampus: DE, drug effects
Hippocampus: ME, metabolism
***Learning: DE, drug effects**
Memory, Short-Term: DE, drug effects
*RNA: BI, biosynthesis
Rats
Tritium
***Uracil Nucleotides: PD, pharmacology**
Visual Perception
RN 10028-17-8 (Tritium); 118-00-3 (Guanosine); 63231-63-0 (RNA)
CN 0 (Uracil Nucleotides)

L97 ANSWER 5 OF 24 MEDLINE on STN
ACCESSION NUMBER: 72186704 MEDLINE
DOCUMENT NUMBER: 72186704 PubMed ID: 5067531
TITLE: [Effect of nucleotide-monophosphates on the acquisition and extinction of conditioned reactions].
Die Wirkung von Nucleotid-Monophosphaten auf die Akquistition und Extinktion bedingter Reaktionen.
AUTHOR: Ott T; Lossner B; Matthies H
SOURCE: PSYCHOPHARMACOLOGIA, (1972) 23 (3) 261-71.
Journal code: 7609417. ISSN: 0033-3158.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197207
ENTRY DATE: Entered STN: 19900310
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Entered Medline: 19720725
CT Check Tags: Animal; Male
Adenosine Monophosphate: PD, pharmacology
Avoidance Learning: DE, drug effects
Behavior, Animal
Cerebral Ventricles
Conditioning (Psychology)
*Conditioning, Classical: DE, drug effects
Cytosine Nucleotides: PD, pharmacology
Discrimination Learning: DE, drug effects
*Extinction (Psychology): DE, drug effects
Guanine Nucleotides: PD, pharmacology
Injections, Spinal
Memory: DE, drug effects
Neurons: ME, metabolism
*Nucleotides: PD, pharmacology
Proteins: BI, biosynthesis
Pyrimidine Nucleotides: PD, pharmacology
RNA: BI, biosynthesis
Rats
Rats, Inbred Strains
Thymine Nucleotides: PD, pharmacology
Uracil Nucleotides: PD, pharmacology
RN **61-19-8 (Adenosine Monophosphate)**; 63231-63-0 (RNA)
CN 0 (Cytosine Nucleotides); 0 (Guanine Nucleotides); 0 (Nucleotides); 0 (Proteins); 0 (Pyrimidine Nucleotides); 0 (Thymine Nucleotides); 0 (Uracil Nucleotides)

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L97 ANSWER 6 OF 24 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2003186082 EMBASE
TITLE: Combined uridine and choline administration improves **cognitive** deficits in spontaneously hypertensive rats.
AUTHOR: De Bruin N.M.W.J.; Kiliaan A.J.; De Wilde M.C.; Broersen L.M.
CORPORATE SOURCE: N.M.W.J. De Bruin, Johnson/Johnson Pharmaceutical R., CNS, Building 10, Turnhoutse weg 30, Beerse B-2340, Netherlands. ndebruin@prdbe.jnj.com
SOURCE: Neurobiology of Learning and Memory, (2003) 80/1 (63-79). Refs: 88
ISSN: 1074-7427 CODEN: NLMEFR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Rationale. Hypertension is considered a risk factor for the development of **cognitive** disorders, because of its negative effects on cerebral vasculature and blood flow. Genetically induced hypertension in rats has been associated with a range of **cognitive** impairments. Therefore, spontaneously hypertensive rats (SHR) can potentially be used as a model for **cognitive** deficits in human subjects. Consecutively, it can be determined whether certain food components can improve **cognition** in these rats. Objective. The present study aimed to determine whether SHR display specific deficits in attention, **learning**, and **memory** function. Additionally, effects of chronic uridine and choline administration were studied. Methods. 5-7 months old SHR were compared with normotensive Wistar-Kyoto (WKY) and Sprague-Dawley (SD) rats. (a) The operant delayed non-matching-to-position (DNMTP) test was used to study short-term **memory** function. (b) The five-choice serial reaction time (5-CSRT) task was used to assess selective visual attention processes. (c) Finally, the Morris water maze (MWM) acquisition was used as a measure for spatial **learning** and mnemonic capabilities. Results. (1) SHR exhibited significantly impaired performance in the 5-CSRT test in comparison with the two other rat strains. Both the SHR and WKY showed deficits in spatial **learning** when compared with the SD rats. (2) Uridine and choline supplementation normalized performance of SHR in the 5-CSRT test. (3) In addition, uridine and choline treatment improved MWM acquisition in both WKY and SHR rats. Conclusion. The present results show that the SHR have a deficiency in visual selective attention and spatial **learning**. Therefore, the SHR may provide an interesting model in the screening of substances with therapeutic potential for treatment of **cognitive** disorders. A combination of uridine and choline administration improved selective attention and spatial **learning** in SHR.

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L97 ANSWER 7 OF 24 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 1999141343 EMBASE
TITLE: Modulation of spontaneous and stimulation-evoked transmitter release from rat sympathetic neurons by the **cognition** enhancer linopirdine: Insights into its mechanisms of action.
AUTHOR: Kristufek D.; Koth G.; Motejlek A.; Schwarz K.; Huck S.;

Boehm S.
CORPORATE SOURCE: Dr. S. Boehm, Institute of Neuropharmacology, University of Vienna, Waehringerstrasse 13a, A-1090 Vienna, Austria
SOURCE: Journal of Neurochemistry, (1999) 72/5 (2083-2091).
Refs: 36
ISSN: 0022-3042 CODEN: JONRA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The mechanisms by which the **cognition** enhancer linopirdine may affect transmitter release were investigated in cultures of rat superior cervical ganglion neurons. Overflow of previously incorporated [3H]noradrenaline evoked by 10 .mu.M UTP or 0.1 .mu.M bradykinin was enhanced by linopirdine at .gtoreq.3 .mu.M, overflow evoked by 25 mM K+, 100 .mu.M nicotine, or 300 .mu.M ATP was enhanced by linopirdine at .gtoreq.10 .mu.M, and overflow due to 40 mM K+ or electrical field stimulation was not altered by linopirdine. Ba2+ (0.3 mM) augmented the same types of stimulation-evoked overflow to a similar extent as linopirdine. K+ (25 mM), nicotine (100 .mu.M), and ATP (300 .mu.M) triggered transmitter release in a partially tetrodotoxin-resistant manner, and the release-enhancing action of linopirdine was lost in the presence of tetrodotoxin (1 .mu.M). Linopirdine (10 .mu.M) raised spontaneous tritium outflow and reduced currents through muscarinic K+ (K(M)) channels with a similar time course. The secretagogue action of linopirdine was concentration- and Ca2+-dependent and abolished by tetrodotoxin (1 .mu.M) or Cd2+ (100 .mu.M). Linopirdine (10 .mu.M) added to the partial inhibition of K(M) channels by 1 or 3 mM Ba2+ but not to the complete inhibition by 10 mM Ba2+. Likewise, the secretagogue action of 1 and 3 mM, but not that of 10 mM, Ba2+ was enhanced by linopirdine. These results indicate that linopirdine facilitates and triggers transmitter release via blockade of K(M) channels and suggest that these K+ channels are located at neuronal somata rather than at presynaptic sites.

=> d ind 7

L97 ANSWER 7 OF 24 EMBASE
on STN
CT Medical Descriptors:
*neurotransmitter release
*sympathetic nerve
***cognition**
concentration response
calcium transport
potassium transport
cellular distribution
membrane electrophysiology
drug mechanism
nonhuman
rat
animal tissue
animal cell
newborn
article
priority journal
Drug Descriptors:
*linopirdine: PD, pharmacology
tetrodotoxin
tritium
barium
noradrenalin: EC, endogenous compound
uridine diphosphate: PD, pharmacology
bradykinin: PD, pharmacology

nicotine: PD, pharmacology
adenosine triphosphate: PD, pharmacology
RN (linopirdine) 105431-72-9; (tetrodotoxin) 4368-28-9, 4664-41-9; (tritium) 10028-17-8; (barium) 7440-39-3; (noradrenalin) 1407-84-7, 51-41-2; (**uridine diphosphate**) 58-98-0; (bradykinin) 58-82-2, 5979-11-3; (nicotine) 54-11-5; (adenosine triphosphate) 15237-44-2, 56-65-5, 987-65-5
CO Sigma (United States); RBI

=> d ibib abs 8

L97 ANSWER 8 OF 24 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 97141555 EMBASE
DOCUMENT NUMBER: 1997141555
TITLE: Developments in purine and pyridimidine receptor-based therapeutics.
AUTHOR: Spedding M.; Williams M.
CORPORATE SOURCE: Dr. M. Williams, Neurological/Urological Dis. Res., Abott Laboratories, 100 Abbott Park, Abbott Park, IL 60064, United States
SOURCE: Drug Development Research, (1996) 39/3-4 (436-441).
Refs: 54
ISSN: 0272-4391 CODEN: DDREDK
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 002 Physiology
005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
016 Cancer
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Progress in the identification of novel P1 and P2 receptor ligands has continued to lag behind the explosion in receptor cloning, especially in the P2 area. Nonetheless, a number of novel chemical entities and natural receptor ligands are continuing to advance in clinical trials or, alternatively have become important new tools to study receptor function. Compounds of note with activity at the P1 receptor family include NNC 21-0136 (A1 agonist; preclinical; stroke); SCH 59761 (nonselective P1 agonist; preclinical; cardiovascular disorders); the A1 antagonists, KFM-19 (BIIP-20; phase II) and MDL 102,503 development (status unknown) that may have therapeutic potential as **cognition** enhancers. KF 17837 and related A(2A)-antagonists such as KW 6002 represent potential novel treatments for Parkinson's disease. SCH 58261 (A(2A) receptor antagonist; preclinical) is a novel nonxanthine antagonist ligand. KW 3902 (phase II), FK- 453/FK 113453 (possibly discontinued) and CVT-124 (phase I) are A1 receptor-selective xanthine-based antagonists that have potential in the treatment of renal diseases. NNC 53-0055 (preclinical) is the first of a new series of selective A3 receptor agonists that modulate cytokine production. MRS 1067, MRS 1067, MRS 1097, MRS 1222, L-249, 313, and L-268, 605 (all preclinical) represent new A3-receptor antagonists. GP 3269 (preclinical) is an adenosine kinase inhibitor with potential efficacy in septic shock, stroke, and pain. ARL 67085 (phase II) is an ATP bioisostere that is an antagonist of the P(2T) receptor that is the first of new generation of antithrombotic agents; Systemic ATP has reached phase II trials as a novel approach to metastasis regression. The pyrimidine nucleotide, UTP (phase II) is being examined as P2Y2 receptor agonist for the treatment of cystic fibrosis.

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L97 ANSWER 8 OF 24 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.

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     on STN
CT   Medical Descriptors:
     *cardiovascular disease
     *central nervous system
       *cognition
     *kidney disease
     *metastasis
     *pain
     *parkinson disease
     *septic shock
     *stroke
     conference paper
     drug research
     human
     nonhuman
     receptor binding
     Drug Descriptors:
     *adenosine kinase inhibitor: AN, drug analysis
     *adenosine kinase inhibitor: CM, drug comparison
     *adenosine kinase inhibitor: DV, drug development
     *adenosine kinase inhibitor: PD, pharmacology
     *adenosine receptor: EC, endogenous compound
     *adenosine receptor stimulating agent: AN, drug analysis
     *adenosine receptor stimulating agent: CM, drug comparison
     *adenosine receptor stimulating agent: DV, drug development
     *adenosine receptor stimulating agent: PD, pharmacology
     *purine p2 receptor: EC, endogenous compound
       *uridine triphosphate: CM, drug comparison
       *uridine triphosphate: PD, pharmacology
RN   (uridine triphosphate) 63-39-8


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L97  ANSWER 9 OF 24  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:        2003:656581  HCAPLUS
DOCUMENT NUMBER:         139:197370
TITLE:                   Preparation of aryl ureas containing pyridine,
                         quinoline and isoquinoline N-oxide functionality as
                         kinase inhibitors
INVENTOR(S):             Dumas, Jacques; Scott, William J.; Riedl, Bernd
PATENT ASSIGNEE(S):      Bayer Corporation, USA
SOURCE:                  PCT Int. Appl., 67 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2003068229      A1   20030821       WO 2003-US4110   20030211
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,
             RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
             NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
             ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                  US 2002-354935P  P  20020211
OTHER SOURCE(S):         MARPAT 139:197370
GI
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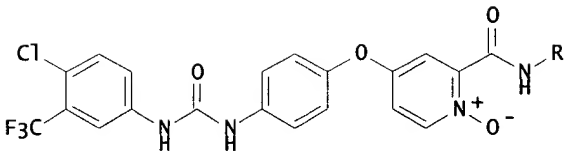


I

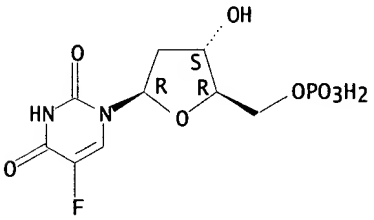
AB The title ureas contg. a pyridine, quinoline, or isoquinoline functionality which is oxidized at the nitrogen heteroatom MLBNHCONHA [A = (un)substituted Ph, naphthyl, 5-6 membered monocyclic heteroaryl, 8-10 membered bicyclic heteroaryl; B = (un)substituted phenylene, naphthylene, 5-6 membered monocyclic heteroarylene, 8-10 membered bicyclic heteroarylene; L = (CH2)mO(CH2)l, (CH2)m(CH2)l, (CH2)mCO(CH2)l, etc.; m, l = 0-4; M = (un)substituted pyridine-1-oxide, quinoline-1-oxide, isoquinoline-1-oxide; with the provisos] which are useful in the treatment of (i) raf mediated diseases, for example, cancer, (ii) p38 mediated diseases such as inflammation and osteoporosis, and (iii) VEGF mediated diseases such as angiogenesis disorders, were claimed. Prepn. of two ureas such as I [R = H, Me] which are not compds. of the invention, and have been distinguished from the compds. of the invention by a proviso, was described. Pharmaceutical compn. comprising the title ureas was claimed.

IT **134-46-3**, 5-Fluorodeoxyuridine monophosphate
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(prepn. of aryl ureas contg. pyridine, quinoline and isoquinoline N-oxide functionality for use in combination with other anti-proliferative agent)

RN 134-46-3 HCAPLUS

CN 5'-Uridylic acid, 2'-deoxy-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L97 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:315467 HCAPLUS
DOCUMENT NUMBER: 136:335248
TITLE: Pyrimidine nucleotide precursors for the treatment of mitochondrial diseases
INVENTOR(S): Von Borstel, Reid W.; Saydoff, Joel A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 39 pp., Cont.-in-part of U. S. Ser. No. 763,955.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002049182	A1	20020425	US 2001-930494	20010816
US 2001005719	A1	20010628	US 1998-144096	19980831
US 6472378	B2	20021029		
WO 2000011952	A1	20000309	WO 1999-US19725	19990831

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

WO 2003015516	A1	20030227	WO 2002-US25831 20020814

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:	US 1998-144096	A2	19980831
	WO 1999-US19725	W	19990831
	US 2001-763955	A2	20010228
	US 2001-930494	A	20010816

AB Compds., compns., and methods are provided for the treatment of disorders related to mitochondrial dysfunction. The methods comprise administering to a mammal a compn. contg. pyrimidine nucleotide precursors in amts. sufficient to treat symptoms resulting from mitochondrial respiratory chain deficiencies.

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L97 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
IC ICM A61K048-00
NCL 514044000
CC 1-10 (Pharmacology)
Section cross-reference(s): 33, 63
ST pyrimidine nucleotide precursor therapeutic mitochondrial respiratory chain deficiency; mitochondrial dysfunction treatment pyrimidine nucleotide precursor
IT Nervous system, disease
(Friedreich's ataxia; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Nervous system, disease
(Huntington's chorea; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Muscle, disease
(Keams-Sayres Syndrome; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Brain, disease
(Leigh's disease; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Brain, disease
(MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes); pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Muscle, disease
(MERRF (myoclonic epilepsy assocd. with ragged-red muscle fibers); pyrimidine nucleotide precursors for the treatment of mitochondrial

diseases)
IT Disease, animal
(NARP (neurogenic muscle weakness, ataxia, and retinitis pigmentosa);; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Eye, disease
(PEO (chronic progressive external ophthalmoplegia); pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Brain, disease
(Rett's Syndrome; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT **Cognition**
(age-related decline in; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Nervous system, disease
(ataxia; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Mental disorder
(attention deficit hyperactivity disorder; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Mental disorder
(autism; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Nervous system, disease
(autonomic neuropathy; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Heart, disease
(cardiomyopathy, dilating; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Muscle
(cells; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Fatigue, biological
(chemotherapy-assocd.; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Menopause
(chemotherapy-induced; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Fatigue, biological
(chronic fatigue syndrome; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Brain
(corpus striatum; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(defective nuclear-encoded, components of the mitochondrial respiratory chain; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Nervous system, disease
(degeneration; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Mutation
(deletion; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Appetite
(depressed; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Mitochondria
(disease, congenital; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Mitochondria
(disease, mitochondrial respiratory chain deficiency; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Development, mammalian postnatal
(disorder, developmental delay in cognitive, motor, language, executive function, or social skills; pyrimidine nucleotide precursors for the

treatment of mitochondrial diseases)
IT Liver, disease
(failure; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Eye, disease
(hereditary optic atrophy; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Acidosis
(lactic; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Behavior
(locomotor; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Headache
(migraine; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Respiration, animal
(mitochondrial, dysfunction, respiratory chain deficiency; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Heart
(myocyte; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Muscular dystrophy
(myotonic; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Bladder, disease
Intestine, disease
(neurogenic, dysfunction; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Nerve
(neuron; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Cell death
(neuronal; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Nerve, disease
(neuropathy, MNGIE (myopathy neuropathy gastrointestinal dysmotility encephalopathy); pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Nerve, disease
(neuropathy, optic nerve (eye); pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Cytoprotective agents
(neuroprotectants; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Toxins
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(neurotoxins; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Hepatitis
(nonalc. steatohepatitis; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Drug delivery systems
(oral; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Nerve, disease
Nerve, disease
(peripheral neuropathy; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Cell
(post-mitotic; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT Aging, animal
Alzheimer's disease
Anti-Alzheimer's agents
Anticonvulsants

Antimigraine agents
Antiparkinsonian agents
Antitumor agents
Antitumor agents
Behavior
Cell death
Chemotherapy
Cognition enhancers
Cytoprotective agents
Death
Disease models
Drug interactions
Epilepsy
Muscular dystrophy
Mutation
Nervous system agents
Neuromuscular diseases
Parkinson's disease
Statistical analysis
(pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT Mitochondrial DNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT **Pyrimidine nucleosides**
Pyrimidine nucleotides
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT Mitochondrial DNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(rearrangement of; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT Acidosis
(renal tubular; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT Deafness
(sensorineural; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT Kidney, disease
(tubular acidosis; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT 33069-62-4, Taxol
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT 51-61-6, Dopamine, biological studies 57-00-1, Creatine 9000-83-3, Complex V (Mitochondrial electron transport) 9001-16-5, Mitochondrial electron transport complex IV 9027-03-6, Mitochondrial electron transport complex III 9028-04-0, Mitochondrial electron transport complex I 9028-11-9, Mitochondrial electron transport complex II
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT 127-17-3, Pyruvic acid, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT 58-96-8DP, **Uridine**, acyl deriv. 65-46-3DP, Cytidine, acyl deriv. 260360-01-8P
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological

study); PREP (Preparation); USES (Uses)
(pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
IT 58-96-8, **Uridine** 65-46-3, Cytidine 65-86-1, Orotic acid
65-86-1D, Orotic acid, esters 127-17-3D, Pyruvic acid, esters
303-98-0, Coenzyme Q10 987-78-0, Cytidine diphosphocholine 1747-53-1,
Ethyl orotate 4105-38-8, 2',3',5'-Tri-O-**acetyluridine**
260360-02-9 260360-03-0 260360-04-1 260360-05-2 260360-06-3
260360-07-4
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

=> d ibib abs hitstr 11

L97 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:208065 HCAPLUS
DOCUMENT NUMBER: 134:242656
TITLE: Phospholipid prodrugs of anti-proliferative drugs
INVENTOR(S): Kozak, Alexander; Shapiro, Israel; Vinnikova, Marina; Ershov, Leonid; Senderikhin, Alexander; Ayalon, Oran
PATENT ASSIGNEE(S): D-Pharm Limited, Israel
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001019320	A2	20010322	WO 2000-IL562	20000913
WO 2001019320	A3	20010927		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000073093	A5	20010417	AU 2000-73093	20000913
EP 1218013	A2	20020703	EP 2000-960946	20000913
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003514770	T2	20030422	JP 2001-522958	20000913
NZ 517522	A	20030829	NZ 2000-517522	20000913
ZA 2002001081	A	20030207	ZA 2002-1081	20020207

PRIORITY APPLN. INFO.: IL 1999-131887 A 19990914
WO 2000-IL562 W 20000913
OTHER SOURCE(S): MARPAT 134:242656

AB The invention discloses prodrugs comprising anti-proliferative drugs covalently linked, via a bridging group, to a phospholipid moiety such that the active species is preferentially released, preferably by enzymic cleavage, at the required site of action. The invention further discloses pharmaceutical compns. comprising said prodrugs and the uses thereof for the treatment of diseases and disorders related to inflammatory, to degenerative or atrophic conditions, and to uncontrolled cell growth. A methotrexate deriv. 1-stearoyl-2-[3-(.alpha.-dodecylate-.gamma.-methotrexate-amido)-propanoyl]-sn-glycero-3-phosphatidylcholine was prepd., and examd. for its inhibitory effect on human leukemia cell growth.

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L97 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
IC ICM A61K
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
ST cell growth inhibitor phospholipid deriv prepn; methotrexate antitumor phospholipid deriv prodrug prepn
IT Antitumor agents
(Burkitt's lymphoma; phospholipid prodrugs of anti-proliferative drugs)
IT Nervous system
(Huntington's chorea, treatment of; phospholipid prodrugs of anti-proliferative drugs)
IT Mental disorder
(Pick's disease, treatment of; phospholipid prodrugs of anti-proliferative drugs)
IT Drug delivery systems
(aerosols; phospholipid prodrugs of anti-proliferative drugs)
IT Nervous system
(amyotrophic lateral sclerosis, treatment of; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(bladder; phospholipid prodrugs of anti-proliferative drugs)
IT Drug delivery systems
(capsules; phospholipid prodrugs of anti-proliferative drugs)
IT Brain, disease
(cerebrovascular, treatment of; phospholipid prodrugs of anti-proliferative drugs)
IT Uterus, neoplasm
(cervix, inhibitors; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(cervix; phospholipid prodrugs of anti-proliferative drugs)
IT Chorion
(choriocarcinoma, inhibitors; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(choriocarcinoma; phospholipid prodrugs of anti-proliferative drugs)
IT Intestine, neoplasm
(colon, inhibitors; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(colon; phospholipid prodrugs of anti-proliferative drugs)
IT Nervous system
(degeneration, treatment of; phospholipid prodrugs of anti-proliferative drugs)
IT Mental disorder
(dementia, multi-infarct, treatment of; phospholipid prodrugs of anti-proliferative drugs)
IT Mental disorder
(dementia, treatment of; phospholipid prodrugs of anti-proliferative drugs)
IT Mental disorder
(dementia, vascular, treatment of; phospholipid prodrugs of anti-proliferative drugs)
IT Nerve, disease
(diabetic neuropathy, treatment of; phospholipid prodrugs of anti-proliferative drugs)
IT Nervous system
(disease, treatment of; phospholipid prodrugs of anti-proliferative drugs)
IT Mycosis
(fungoides, inhibitors; phospholipid prodrugs of anti-proliferative drugs)
IT Drug delivery systems
(gels; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(head; phospholipid prodrugs of anti-proliferative drugs)
IT Liver, neoplasm

(hepatoma, inhibitors; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(hepatoma; phospholipid prodrugs of anti-proliferative drugs)
IT Neoplasm
(hydatidiform mole, treatment of; phospholipid prodrugs of anti-proliferative drugs)
IT Intestine, disease
(inflammatory bowel syndromes, treatment of; phospholipid prodrugs of anti-proliferative drugs)
IT Intestine, neoplasm
Lung, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Skin, neoplasm
(inhibitors; phospholipid prodrugs of anti-proliferative drugs)
IT Drug delivery systems
(injections, i.v.; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(intestine; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(lung; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(lymphocytic leukemia; phospholipid prodrugs of anti-proliferative drugs)
IT Eye, disease
(macula, degeneration, age-related, treatment of; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(mammary gland; phospholipid prodrugs of anti-proliferative drugs)
IT Headache
(migraine, treatment of; phospholipid prodrugs of anti-proliferative drugs)
IT Skin, neoplasm
(mycosis fungoides, inhibitors; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(mycosis fungoides; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(myelogenous leukemia; phospholipid prodrugs of anti-proliferative drugs)
IT Drug delivery systems
(nasal; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(neck; phospholipid prodrugs of anti-proliferative drugs)
IT Bladder
Head
Mammary gland
Neck, anatomical
Prostate gland
Urinary tract
(neoplasm, inhibitors; phospholipid prodrugs of anti-proliferative drugs)
IT Trophoblast
(neoplasm, treatment of; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(non-Hodgkin's lymphoma; phospholipid prodrugs of anti-proliferative drugs)
IT Drug delivery systems
(ointments; phospholipid prodrugs of anti-proliferative drugs)
IT Drug delivery systems
(ophthalmic; phospholipid prodrugs of anti-proliferative drugs)
IT Nerve
(optic, treatment of; phospholipid prodrugs of anti-proliferative drugs)
IT Drug delivery systems

(oral; phospholipid prodrugs of anti-proliferative drugs)
IT Pharynx
(oropharynx carcinoma, inhibitors; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(oropharynx carcinoma; phospholipid prodrugs of anti-proliferative drugs)
IT Bone, neoplasm
(osteosarcoma, inhibitors; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(osteosarcoma; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(ovary; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(pancreas; phospholipid prodrugs of anti-proliferative drugs)
IT Drug delivery systems
(parenterals; phospholipid prodrugs of anti-proliferative drugs)
IT **Anti-Alzheimer's agents**
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antiparkinsonian agents
Antirheumatic agents
Antitumor agents
(phospholipid prodrugs of anti-proliferative drugs)
IT **Lysophosphatidylcholines**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of phospholipid prodrugs of anti-proliferative drugs)
IT Drug delivery systems
(prodrugs; phospholipid prodrugs of anti-proliferative drugs)
IT Proliferation inhibition
(proliferation inhibitors; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(prostate gland; phospholipid prodrugs of anti-proliferative drugs)
IT Drug delivery systems
(rectal; phospholipid prodrugs of anti-proliferative drugs)
IT Connective tissue
(scleroderma, treatment of; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(skin; phospholipid prodrugs of anti-proliferative drugs)
IT Drug delivery systems
(solns.; phospholipid prodrugs of anti-proliferative drugs)
IT Brain, disease
(stroke, treatment of; phospholipid prodrugs of anti-proliferative drugs)
IT Drug delivery systems
(suppositories; phospholipid prodrugs of anti-proliferative drugs)
IT Drug delivery systems
(suspensions; phospholipid prodrugs of anti-proliferative drugs)
IT Lupus erythematosus
(systemic, treatment of; phospholipid prodrugs of anti-proliferative drugs)
IT Drug delivery systems
(tablets; phospholipid prodrugs of anti-proliferative drugs)
IT Drug delivery systems
(topical; phospholipid prodrugs of anti-proliferative drugs)
IT Granulomatous disease
Multiple sclerosis
Psoriasis
(treatment of; phospholipid prodrugs of anti-proliferative drugs)
IT Antitumor agents
(urinary tract; phospholipid prodrugs of anti-proliferative drugs)
IT 9001-84-7, Phospholipase A2 9013-93-8, Phospholipase
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(activated by; phospholipid prodrugs of anti-proliferative drugs)
IT 330658-48-5P 330658-49-6P 330658-50-9P 330658-51-0P 330658-52-1P
330658-55-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of phospholipid prodrugs of anti-proliferative drugs)
IT 330658-53-2 330658-54-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of phospholipid prodrugs of anti-proliferative drugs)
IT 50-91-9, 5-Fluoro-2'-**deoxyuridine** 56-12-2, 4-Aminobutanoic acid, reactions 59-05-2, Methotrexate 60-32-2, 6-Aminohexanoic acid 64-19-7, Acetic acid, reactions 76-83-5, Trityl chloride 107-95-9, 3-Aminopropanoic acid 123-76-2, Levulinic acid 501-53-1, Benzyl chloroformate 660-88-8, 5-Aminovaleric acid 1002-57-9, 8-Aminooctanoic acid 1069-66-5, Sodium 2-Propylpentanoate 4160-82-1, 3,3-Dimethylglutaric anhydride 19420-57-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of phospholipid prodrugs of anti-proliferative drugs)
IT 1947-00-8P, 6-[N-(Benzyloxycarbonyl)amino]hexanoic acid 2304-94-1P 5066-71-7P 5105-78-2P 10343-71-2P 23135-50-4P 23434-40-4P 57444-77-6P 76523-73-4P 93349-30-5P 112489-84-6P 163225-49-8P 271781-53-4P 330658-56-5P 330658-57-6P 330658-58-7P 330658-59-8P 330658-60-1P 330658-62-3P 330658-64-5P 330658-66-7P 330658-68-9P 330658-69-0P 330658-70-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of phospholipid prodrugs of anti-proliferative drugs)

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L97 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:703740 HCAPLUS
DOCUMENT NUMBER: 135:251986
TITLE: Methods for treating fibroproliferative diseases with antiproliferative or antifibrotic agents, especially antisense c-Jun oligonucleotides
INVENTOR(S): Peterson, Theresa C.
PATENT ASSIGNEE(S): Dalhousie University, Can.
SOURCE: U.S., 13 pp., Cont.-in-part of U.S. 6,025,151.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6294350	B1	20010925	US 1999-433621	19991102
US 5985592	A	19991116	US 1997-870096	19970605
US 6025151	A	20000215	US 1998-92317	19980605
WO 2001032156	A2	20010510	WO 2000-IB1731	20001102
WO 2001032156	A3	20020926		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1997-870096 A2 19970605
US 1998-92317 A2 19980605

US 1999-433621 A1 19991102

AB In accordance with the present invention, fibroproliferative disease or condition characterized by such symptoms as increased levels of c-Jun homodimers, increased heterodimerization of c-Jun with another signaling peptide, increased levels of phosphorylated c-Jun, or increased presence of Jun kinase are treated by administering to the subject an amt. of a compd. effective to ameliorate one or more of the symptoms of the disease or condition, for example, an antiproliferative or antifibrotic agent. Preferred compds. for administration according to the invention are antisense c-Jun oligonucleotides and compds. that block c-Jun phosphorylation, such as pentoxifylline, or a functional deriv. or metabolite thereof. Also provided by the present invention are in vitro tests for identifying whether a test compd. is useful for treatment of a subject afflicted with such a disease and kits useful for conducting such assays.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L97 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
IC ICM C12Q001-02
ICS C12Q001-00; C12Q001-50
NCL 435029000
CC 1-12 (Pharmacology)
Section cross-reference(s): 9, 63
ST fibroproliferative disease treatment antiproliferative antifibrotic agent; antiproliferative antisense oligonucleotide fibroproliferative disease cJun
IT Peptides, biological studies
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ATF2; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Angiotensin receptors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AT1, inhibitors; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Hepatitis
(C; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Transcription factors
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(CREB (cAMP-responsive element-binding); antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Eye, disease
Graves' disease
(Graves' ophthalmopathy; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Sarcoma
(Kaposi's; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Neoplasm
(Li-Fraumeni syndrome; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Transcription factors
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence);

BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(NF-.kappa.B (nuclear factor .kappa.B); antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Peptides, biological studies
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Nrf1; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Eye
(Tenon's capsule, fibroproliferation; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Leukemia
(acute myelogenous; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Abdomen
(adhesions; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Fibrosis
(antifibrotics; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Alzheimer's disease
Animal tissue culture
Anti-Alzheimer's agents
Antitumor agents
Drug screening
Epithelium
Fibroblast
Hematopoietic precursor cell
Keloid
Kidney, disease
Leprosy
Mesenchyme
Multiple sclerosis
Myelodysplastic syndromes
Myeloproliferative disorders
Neoplasm
Neuroglia
Phosphorylation, biological
Picrorhiza kurroa
Signal transduction, biological
Silicosis
Silybum marianum
Test kits
(antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Platelet-derived growth factors
Tumor necrosis factors
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Antisense oligonucleotides
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Decorins
Phosphatidylcholines, biological studies
Tocopherols

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Bronchi
(bronchiolitis, obliterative; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Signal peptides
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(c-Jun heterodimerization with; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Transcription factors
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process)
(c-jun; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Malaria
(cerebral; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Intestine, disease
(colitis, collagenous; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Cardiovascular system
(disease; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Drugs
Ergot (Claviceps)
(drug-induced ergotism; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Reproductive tract
(female, cancer; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Intestine
Lung
Skin
(fibroblasts of; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Radiation
(fibrosis from; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Heart, disease
Kidney, disease
Liver, disease
Lung, disease
Peritoneum
(fibrosis; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Gene, animal
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(for c-Jun; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Neuroglia

(glioblastoma, sporadic; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Neuroglia
(glioblastoma; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Kidney, disease
(glomerulonephritis; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Neutrophil
(infiltration; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Intestine, disease
(inflammatory; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Cytokines
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(inflammatory; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Drug delivery systems
(inhalants; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Drug delivery systems
(injections, i.m.; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Drug delivery systems
(injections, i.v.; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Lung, disease
(interstitial; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Brain, disease
(malaria; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Antitumor agents
(mammary gland; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Kidney
(mesangium; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Leukemia
(myelogenous; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Liver
(myofibroblasts of; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Mammary gland
(neoplasm, inhibitors; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Mammary gland
(neoplasm; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Nerve, neoplasm
(neuroblastoma; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
IT Drug delivery systems
(oral; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Proteins, specific or class
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(p65, NF-.kappa.B p65; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT **Phosphatidylcholines, biological studies**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyenyl-; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Proliferation inhibition
(proliferation inhibitors; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Disease, animal
(proliferative; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Drug delivery systems
(rectal; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Connective tissue
(scleroderma; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Shock (circulatory collapse)
(septic; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Blood vessel
(smooth muscle; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Muscle
(smooth; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Carcinoma
(squamous cell, differentiation disorder; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Cell differentiation
(squamous cell, disorder; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Drug delivery systems
(sustained-release; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Lupus erythematosus
(systemic, nephritis assocd. with; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Drug delivery systems
(topical; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Drug delivery systems
(transdermal; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Interferons
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.alpha.; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Transforming growth factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.-, RII/FC; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT 155215-87-5, Jun kinase
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT 217308-10-6, DNA, d(G-C-A-G-T-C-A-T-A-G-A-A-C-A-G-T-C-C-G-T-C-A-C-T-T-C-A-C-G-T)
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT 50-23-7, Hydrocortisone 54-85-3, Isoniazid 54-85-3D, Isoniazid, conjugated 59-67-6, Niacin, biological studies 64-86-8, Colchicine 107-35-7, Taurine 518-34-3, Tetrandrine 1028-33-7, Pentifylline 1405-86-3, Glycyrrhizin 6493-05-6, Pentoxifylline 6493-05-6D, Pentoxifylline, derivs. and metabolites 6493-06-7, 1H-Purine-2,6-dione, 3,7-dihydro-1-(5-hydroxyhexyl)-3,7-dimethyl- 10102-43-9, Nitric oxide, biological studies 53179-13-8, Pirfenidone 55242-55-2, Propentofylline 55837-20-2, Halofuginone 62571-86-2, Captopril 75847-73-3, Enalapril 80288-49-9, Furafylline 83150-76-9, Octreotide 85721-33-1, Ciprofloxacin 91161-71-6, Terbinafine 114798-26-4, Losartan 119290-87-8, Acanthoic acid 120210-48-2, Tenidap
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT 50-88-4, Tritiated thymidine, biological studies 1148-63-6, Thymidine-.alpha.-t 42459-79-0, **Uridine**, 5-bromo-, labeled with tritium
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT 330196-64-0, Cytochrome p 450 1A2
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(inhibitors; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT 9015-82-1, Angiotensin converting enzyme
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

=> d ibib abs hitstr 13

L97 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:624138 HCAPLUS
DOCUMENT NUMBER: 135:175416
TITLE: Uridylic acid, guanylic acid, uridine and/or guanosine for improving learning and **memory** functions
INVENTOR(S): Azehiru, Toichi; Endo, Kazuki; Miyazaki, Shuichi
PATENT ASSIGNEE(S): Yamasa Shoyu Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent

LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001233776	A2	20010828	JP 2000-48714	20000225

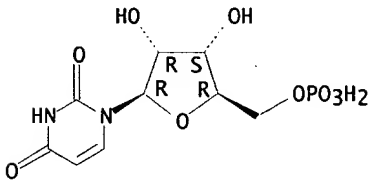
PRIORITY APPLN. INFO.: JP 2000-48714 20000225

AB Uridylic acid, guanylic acid, uridine and/or guanosine are claimed as health foods for improving learning and memory functions esp. for Alzheimer's disease. The learning- and memory-enhancing effects were tested in aged rats.

IT **58-97-9**, Uridylic acid, biological studies
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(uridylic acid, guanylic acid, uridine and/or guanosine for improving learning and memory functions)

RN 58-97-9 HCAPLUS
CN 5'-Uridylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L97 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:608584 HCAPLUS
DOCUMENT NUMBER: 133:187987
TITLE: Methods using pyrimidine-based nucleosides for treatment of mitochondrial disorders
INVENTOR(S): Naviaux, Robert K.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050043	A1	20000831	WO 2000-US4663	20000223
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
NZ 513926	A	20010928	NZ 2000-513926	20000223
BR 2000008447	A	20020115	BR 2000-8447	20000223
EP 1171137	A1	20020116	EP 2000-910321	20000223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

JP 2002537340 T2 20021105 JP 2000-600654 20000223
PRIORITY APPLN. INFO.: US 1999-121588P P 19990223
WO 2000-US4663 W 20000223
OTHER SOURCE(S): MARPAT 133:187987
AB Methods are provided for the treatment of mitochondrial disorders. The methods include the administration of a pyrimidine-based nucleoside, e.g. **triacetyluridine**. Also provided are methods of reducing or eliminating symptoms assocd. with mitochondrial disorders. Mitochondrial disorders particularly appropriate for treatment include those attributable to a deficiency of one or more pyrimidines.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L97 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
IC ICM A61K031-70
CC 1-12 (Pharmacology)
ST pyrimidine nucleoside deriv mitochondrial disorder treatment; **triacetyluridine** mitochondrial disorder treatment
IT Transport proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ADP/ATP carrier, deficiency; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Disease, animal
(Alpers syndrome; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Disease, animal
(Asperger syndrome with declines during infection; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Nervous system
(Huntington's chorea; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Muscle, disease
(Kearns-Sayre syndrome; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Brain, disease
(Leigh's disease; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Disease, animal
(MARIAHS; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Brain, disease
(MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes); pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Muscle, disease
(MERRF (myoclonic epilepsy assocd. with ragged-red muscle fibers); pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Disease, animal
(MNGIE; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Disease, animal
(NARP/MILS; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Bone marrow, disease
Pancreas, disease
(Pearson marrow-pancreas syndrome; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Disease, animal
(Wolfram syndrome; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Antibiotics
(aminoglycoside, deafness assocd. with; pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT Deafness
(aminoglycoside-assocd.; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Nervous system
(amyotrophic lateral sclerosis; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Vitamins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and cofactors; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Mental disorder
(attention deficit hyperactivity disorder; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Mental disorder
(autism, autism with declines during infection; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Carboxylic acids, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(carboxylic aciduria, ethylmalonic aciduria with lactic acidemia; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Heart, disease
(cardiomyopathy; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Movement disorders
(cerebral palsy, with declines during infection; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Eye, disease
(chronic progressive external ophthalmoplegia; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Antiemetics
(cyclic vomiting syndrome with declines during infection; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Cardiolipins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(deficiency; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Mental disorder
(dementia; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Antidiabetic agents
(diabetes mellitus lactic acidemia; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Carboxylic acids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dicarboxylic, pyrimidine nucleoside derivs.; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Heart, disease
(dilated cardiomyopathy; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Mitochondria
(diseases; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT **Learning**
(disorder, dyslexia, with declines during infection; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Toxicity
(drug; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Nervous system
(dystonia, ND6; pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT Necrosis
(familial bilateral striatal; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Eye, disease
(hereditary optic atrophy; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Eye, disease
(impaired eyesight; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Acidosis
(lactic, ethylmalonic aciduria with lactic acidemia; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Antitumor agents
(leukemia, thrombocytopenia and leukemia syndrome; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Spleen, neoplasm
Spleen, neoplasm
(lymphoma, inhibitors; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Disease, animal
(mtDNA depletion syndrome; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Disease, animal
(multiple mtDNA deletion syndrome; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT DNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(nuclear; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Enzymes, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(of pyrimidine synthetic pathway; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Amino acids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pyrimidine nucleoside derivs.; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Pyrimidine bases
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(pyrimidine synthetic pathway; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Anticonvulsants
Cardiovascular agents
Mutation
(pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT **Pyrimidine nucleosides**
Ubiquinones
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Mitochondrial DNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Infection
(refractory epilepsy or Asperger syndrome or autism with declines during infection; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Acidosis

(renal tubular; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Muscle, disease
(skeletal and peripheral and autonomic; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Antitumor agents
(spleen lymphoma; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Platelet (blood)
(thrombocytopenia, thrombocytopenia and leukemia syndrome; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Kidney, disease
(tubular acidosis; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT Nervous system agents
(**uridine**-responsive neurol. syndrome; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT 300-85-6, 3-Hydroxybutyric acid
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(3-hydroxybutyric aciduria with lactic acidemia; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT 5746-90-7, 3-Methylglutaconic acid
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(3-methylglutaconic aciduria with lactic acidemia; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT 9000-83-3, Complex V (mitochondrial electron transport) 9001-16-5, Complex IV (mitochondrial electron transport) 9002-02-2, Succinate dehydrogenase 9014-20-4, Pyruvate dehydrogenase 9027-03-6, Complex III (mitochondrial electron transport) 9028-04-0, Complex I (mitochondrial electron transport) 9028-11-9, Complex II (mitochondrial electron transport)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(deficiency; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT 601-75-2, Ethylmalonic acid
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ethylmalonic aciduria with lactic acidemia; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT 51-35-4, Hydroxyproline
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(hydroxyprolinuria; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT 9001-92-7, Protease 9068-38-6, Reverse transcriptase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT 3056-17-5, Stavudine 7481-89-2, Zalcitabine 30516-87-1, Azidothymidine 69123-98-4, FIAU 69655-05-6, Didanosine 75706-12-6, Leflunomide 96187-53-0, Brequinar 127779-20-8, Saquinavir 150378-17-9, Indinavir 155213-67-5, Ritonavir 159989-64-7, Nelfinavir
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT 9029-03-2, Dihydroorotate dehydrogenase 74870-74-9, **Uridine** monophosphate synthase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pyrimidine-based nucleoside for treatment of mitochondrial disorder)
IT 51-35-4D, L-Hydroxyproline, pyrimidine nucleoside derivs. 52-90-4D, L-Cysteine, pyrimidine nucleoside derivs., biological studies 56-40-6D, Glycine, pyrimidine nucleoside derivs., biological studies 56-41-7D, L-Alanine, pyrimidine nucleoside derivs., biological studies 56-45-1D,

L-Serine, pyrimidine nucleoside derivs., biological studies 56-84-8D, L-Aspartic acid, pyrimidine nucleoside derivs., biological studies 56-86-0D, L-Glutamic acid, pyrimidine nucleoside derivs., biological studies 56-87-1D, L-Lysine, pyrimidine nucleoside derivs., biological studies 56-89-3D, L-Cystine, pyrimidine nucleoside derivs., biological studies 58-85-5, Biotin 59-30-3, Folic acid, biological studies 59-43-8, Vitamin B1, biological studies 59-67-6, Niacin, biological studies 60-18-4D, L-Tyrosine, pyrimidine nucleoside derivs., biological studies 61-90-5D, L-Leucine, pyrimidine nucleoside derivs., biological studies 68-19-9, Vitamin B12 70-26-8D, L-Ornithine, pyrimidine nucleoside derivs. 71-00-1D, L-Histidine, pyrimidine nucleoside derivs., biological studies 72-18-4D, L-Valine, pyrimidine nucleoside derivs., biological studies 72-19-5D, L-Threonine, pyrimidine nucleoside derivs., biological studies 73-32-5D, L-Isoleucine, pyrimidine nucleoside derivs., biological studies 74-79-3D, L-Arginine, pyrimidine nucleoside derivs., biological studies 79-83-4, Pantothenic acid 83-88-5, Vitamin B2, biological studies 147-85-3D, L-Proline, pyrimidine nucleoside derivs., biological studies 541-15-1D, L-Carnitine, pyrimidine nucleoside derivs. 4105-38-8 8059-24-3, Vitamin B6 52009-14-0, Calcium pyruvate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT 71-52-3, Bicarbonate, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT 58-96-8, **Uridine**
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(pyrimidine-based nucleoside for treatment of mitochondrial disorder)

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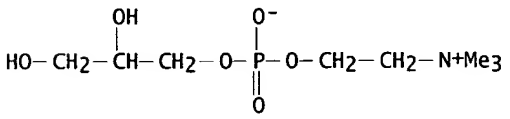
L97 ANSWER 15 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:98343 HCAPLUS
DOCUMENT NUMBER: 132:132349
TITLE: Methods using **uridine** or a **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human neurological diseases
INVENTOR(S): Watkins, Carol; Wurtman, Richard J.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006174	A1	20000210	WO 1999-US17235	19990730
W: CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2339008	AA	20000210	CA 1999-2339008	19990730
EP 1140104	A1	20011010	EP 1999-937631	19990730
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 2002028787	A1	20020307	US 1999-363748	19990730
JP 2003517437	T2	20030527	JP 2000-562028	19990730
PRIORITY APPLN. INFO.:			US 1998-95002P P	19980731
			WO 1999-US17235 W	19990730

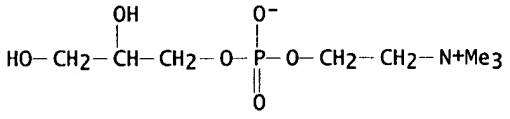
AB Methods of treating certain neurol. diseases using exogenous **uridine** or a **uridine** source alone as a precursor of endogenous cytidine, particularly in the human brain, are disclosed. Methods are also disclosed in which exogenous **uridine** or a **uridine** source is combined either with drugs increasing **uridine** availability or with compds. that serve as a source of choline in phospholipid synthesis.

IT **563-24-6**, Glycerophosphatidylcholine **563-24-6D**, Glycerophosphocholine, acyl derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human neurol. diseases)

RN 563-24-6 HCAPLUS
CN Ethanaminium, 2-[[(2,3-dihydroxypropoxy)hydroxyphosphinyl]oxy]-N,N,N-trimethyl-, inner salt (9CI) (CA INDEX NAME)



RN 563-24-6 HCAPLUS
CN Ethanaminium, 2-[[(2,3-dihydroxypropoxy)hydroxyphosphinyl]oxy]-N,N,N-trimethyl-, inner salt (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L97 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:798788 HCAPLUS
DOCUMENT NUMBER: 130:148627
TITLE: Effects of nucleotides on learning and **memory** in a morris water maze test in normal and basal forebrain-lesioned rats
AUTHOR(S): Miyazaki, Shuichi; Imaizumi, Masahiro; Abiru, Toichi; Machida, Haruhiko
CORPORATE SOURCE: Biology Laboratory, Yamasa Corporation, Chiba, 288-0056, Japan
SOURCE: Life Sciences (1998), Volume Date 1999, 64(1), 45-52
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

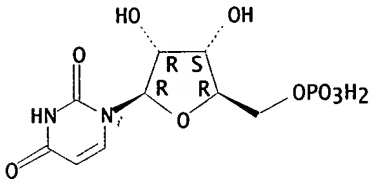
AB The effects of nucleotides on learning and **memory** were studied in normal and basal forebrain-lesioned rats using a Morris water maze test. Chronic oral administration of a nucleotide mixt. (500 mg/kg), contg. an equal wt. of the disodium salts of AMP, GMP, IMP, CMP, and UMP, facilitated learning acquisition in normal rats. In basal forebrain-lesioned rats, administration of the nucleotide mixt. showed a tendency to improve learning acquisition and **memory** retrieval. In the biochem. studies, no significant changes were obsd. in brain

choline and acetylcholine levels by treatment with the nucleotide mixt. at the doses tested in both normal and basal forebrain-lesioned rats. The nucleotides did not affect the monoaminergic systems in normal rats, but did cause some changes in these systems in basal forebrain-lesioned rats. The present studies indicate that nucleotides ameliorate learning and **memory** processes in normal rats, but not in basal forebrain-lesioned rats, and they also modulate the activity of the central monoaminergic systems under certain conditions.

IT **58-97-9**, 5'-UMP, biological studies
RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(effects of nucleotides on learning and **memory** in Morris water maze test in normal and basal forebrain-lesioned rats)

RN 58-97-9 HCAPLUS
CN 5'-Uridylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ind 16

L97 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
CC 1-11 (Pharmacology)
ST nucleotide learning **memory** forebrain lesion; monoaminergic system brain nucleotide
IT **Learning**
Memory, biological
(effects of nucleotides on learning and **memory** in Morris water maze test in normal and basal forebrain-lesioned rats)
IT Nucleotides, biological studies
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of nucleotides on learning and **memory** in Morris water maze test in normal and basal forebrain-lesioned rats)
IT Neurotransmitters
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(effects of nucleotides on learning and **memory** in Morris water maze test in normal and basal forebrain-lesioned rats)
IT Brain, disease
(lesion, fore-; effects of nucleotides on learning and **memory** in Morris water maze test in normal and basal forebrain-lesioned rats)
IT Brain
(monoaminergic system; effects of nucleotides on learning and **memory** in Morris water maze test in normal and basal forebrain-lesioned rats)
IT **58-97-9**, 5'-UMP, biological studies 61-19-8, 5'-AMP, biological studies 63-37-6, 5'-CMP 85-32-5, 5'-GMP 131-99-7, 5'-IMP
RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(effects of nucleotides on learning and **memory** in Morris water maze test in normal and basal forebrain-lesioned rats)

IT 50-67-9, Serotonin, biological studies 51-41-2, Noradrenaline 51-61-6, Dopamine, biological studies 54-16-0, 5-HIAA, biological studies 102-32-9, DOPAC 306-08-1, HVA 534-82-7, 3-Methoxy-4-hydroxy-phenylethylene glycol
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(effects of nucleotides on learning and **memory** in Morris water maze test in normal and basal forebrain-lesioned rats)

=> d ibib abs hitstr 17

L97 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:234128 HCAPLUS
DOCUMENT NUMBER: 126:229629
TITLE: Purine nucleosides and pyrimidine nucleosides for the treatment of memory loss
INVENTOR(S): Yamamoto, Shigeru
PATENT ASSIGNEE(S): Otsuka Pharma Co Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09030976	A2	19970204	JP 1995-179886	19950717

PRIORITY APPLN. INFO.: JP 1995-179886 19950717
AB An agent for improving memory loss comprises a purine nucleoside and a pyrimidine nucleoside. The claimed agent contains inosine, cytidine, **uridine**, guanosine-5'-phosphate, and thymidine at the mol ratio of 4:4:3:4:1.

=> d ind 17

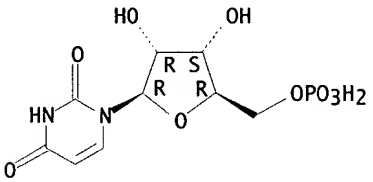
L97 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
IC ICM A61K031-70
ICS C07H019-067; C07H019-167; C07H019-20
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
ST memory improvement purine pyrimidine nucleoside; inosine cytidine **uridine** guanosine thymidine dementia
IT Drug delivery systems
(injections; memory loss treatment with purine nucleoside and pyrimidine nucleoside)
IT **Amnesia**
(memory loss treatment with purine nucleoside and pyrimidine nucleoside)
IT Purine nucleosides
Pyrimidine nucleosides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(memory loss treatment with purine nucleoside and pyrimidine nucleoside)
IT Drug delivery systems
Drug delivery systems
(powders, oral; memory loss treatment with purine nucleoside and pyrimidine nucleoside)
IT Mental disorder
(senile psychosis; memory loss treatment with purine nucleoside and pyrimidine nucleoside)

IT 50-89-5, Thymidine, biological studies 58-63-9, Inosine 58-96-8, **Uridine** 65-46-3, Cytidine 85-32-5, Guanosine 5'-phosphoric acid 118-00-3, Guanosine, biological studies 5550-12-9, 5'-GMP disodium salt
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(memory loss treatment with purine nucleoside and pyrimidine nucleoside)

=> d ibib abs hitstr 18

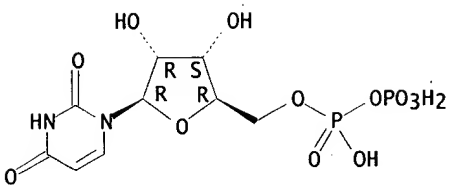
L97 ANSWER 18 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1990:417462 HCAPLUS
DOCUMENT NUMBER: 113:17462
TITLE: Metabolization of a retention-improving dosage of methylglucamine orotate in rat brain
AUTHOR(S): Staak, S.; Tischmeyer, W.; Popov, N.; Matthies, H.
CORPORATE SOURCE: Inst. Neurobiol. Brain Res., Acad. Sci. GDR, Magdeburg, 3090, Ger. Dem. Rep.
SOURCE: Biomedica Biochimica Acta (1990), 49(4), 257-62
CODEN: BBIADT; ISSN: 0232-766X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study was carried out to investigate the time course of metab. in brain and the influence on RNA synthesis of a retention-improving dosage of methylglucamine orotate after intracerebroventricular application. As detd. by the HPLC technique, 73% of acid-sol. radioactivity was recovered in unmetabolized orotic acid 30 min after injection of 1 .mu.mole methylglucamine [6-14C]orotate. Two hours later the amt. of radioactivity found in this compd. was negligible. Anal. of the sequence of labeling of uridine compds. revealed uridine to be the metabolite exhibiting the highest radioactivity at 30 min, whereas UMP- and UDP-sugars attained their max. 90 min after injection of the precursor. Incorporation of [3H]guanosine into brain RNA was not altered by intraventricular application of 1 .mu.mole methylglucamine orotate as compared to methylglucamine chloride-treated controls. The results are interpreted in the light of behavioral findings in which the pyrimidine nucleotide precursor at the dosage used improved the retention performance of an acquired behavior in the rat.
IT **58-97-9**, UMP, biological studies **58-98-0**, UDP, biological studies **63-39-8**, UTP
RL: BIOL (Biological study)
(as methylglucamine orotate metabolite, in brain, memory improvement in relation to)
RN 58-97-9 HCAPLUS
CN 5'-Uridylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



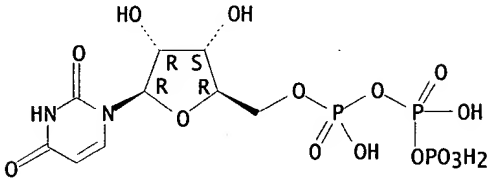
RN 58-98-0 HCAPLUS
CN Uridine 5'-(trihydrogen diphosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 63-39-8 HCAPLUS
CN Uridine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

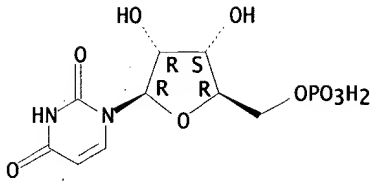
Absolute stereochemistry.



=> d ibib abs hitstr 19

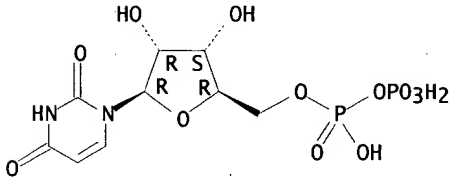
L97 ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:151896 HCAPLUS
DOCUMENT NUMBER: 110:151896
TITLE: Amnestic action of 2-deoxy-D-galactose is not related to a uridylate trapping effect
AUTHOR(S): Schmidt, S.; Richter, P.; Staak, S.; Grecksch, G.; Popov, N.; Jork, R.; Matthies, H.
CORPORATE SOURCE: Inst. Pharmacol. Toxicol., Med. Acad., Magdeburg, 3090, Ger. Dem. Rep.
SOURCE: Neuroscience Research Communications (1989), 4(1), 1-10
CODEN: NRCOEE; ISSN: 0893-6609
DOCUMENT TYPE: Journal
LANGUAGE: English
AB When rats were trained on a brightness discrimination task, intrahippocampal injections of 2-deoxy-D-galactose caused a strong amnesia, measured as an impaired retention performance in a relearning session carried out 24 h later. This amnestic action is not related to a uridylate trapping effect induced by the deoxy-sugar, since the values of hippocampal uridine phosphates were similar to those obtained from saline-treated control animals. Therefore, the prevention of amnesia by a pretrial i.p. injection of methylglucamine orotate, known to improve long-term memory formation, seems not to be due to a substitution of trapped pyrimidine nucleotides. More likely, methylglucamine orotate accelerates the mol. mechanisms underlying the formation of a memory trace. Thus, it prevents at crit. times during memory processing those structural and(or) functional modifications of certain glycoconjugates induced by an incorporation of 2-deoxy-D-galactose into carbohydrate chains and assumed to interfere with long-term memory formation.
IT **58-97-9**, 5'-UMP, biological studies **58-98-0**, 5'-UDP, biological studies **63-39-8**, 5'-UTP
RL: BIOL (Biological study)
(of brain hippocampus, deoxygalactose effect on, long-term memory formation in relation to)
RN 58-97-9 HCAPLUS
CN 5'-Uridylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



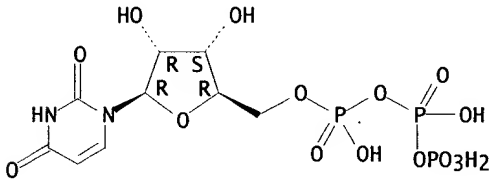
RN 58-98-0 HCAPLUS
CN Uridine 5'-(trihydrogen diphosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 63-39-8 HCAPLUS
CN Uridine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

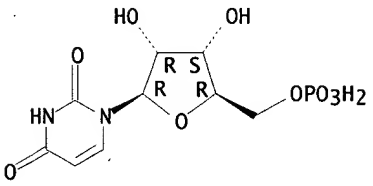
Absolute stereochemistry.



=> d ibib abs hitstr 20

L97 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1974:411252 HCAPLUS
DOCUMENT NUMBER: 81:11252
TITLE: Brain uridine monophosphate. Reduced incorporation of uridine during avoidance learning
AUTHOR(S): Entingh, Dan; Damstra-Entingh, Terri; Dunn, Adrian; Wilson, John Eric; Glassman, Edward
CORPORATE SOURCE: Sch. Med., Univ. North Carolina, Chapel Hill, NC, USA
SOURCE: Brain Research (1974), 70(1), 131-8
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Avoidance training produced no detectable changes in the radioactivity incorporated from uridine-5-3H into total RNA of mouse brain, but decreased the radioactivity in brain UMP. The chem. response was largest in the subcortical forebrain, and did not occur in yoked control mice. This phenomenon has important implications for the interpretation of previous expts., which employed the amt. of radioactivity in UMP as the pool correction factor in studying the effects of avoidance training upon the incorporation of uridine into brain RNA.
IT **58-97-9**, biological studies
RL: FORM (Formation, nonpreparative)
(formation of, by brain in learning)
RN 58-97-9 HCAPLUS
CN 5'-Uridylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



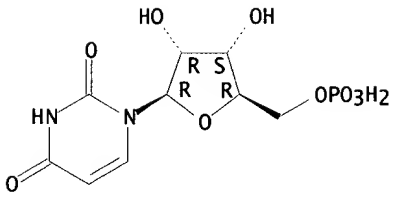
=> d ind 20

L97 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
CC 13-2 (Mammalian Biochemistry)
ST learning brain RNA biosynthesis; **memory** brain uridine metab
IT **Learning**
(UMP formation by brain in)
IT Brain, metabolism
(UMP formation by, in learning)
IT Ribonucleic acids
RL: FORM (Formation, nonpreparative)
(formation of, by brain in learning)
IT **58-97-9**, biological studies
RL: FORM (Formation, nonpreparative)
(formation of, by brain in learning)

=> d ibib abs hitstr 21

L97 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1973:119731 HCAPLUS
DOCUMENT NUMBER: 78:119731
TITLE: Effects of RNA precursors on development and maintenance of long-term **memory**. Hippocampal and cortical pre- and post-training application of RNA precursors
AUTHOR(S): Ott, Tilmann; Matthies, Hanjuergen
CORPORATE SOURCE: Inst. Pharmakol. Toxikol., Med. Akad., Magdeburg, Ger. Dem. Rep.
SOURCE: Psychopharmacologia (1973), 28(2), 195-204
CODEN: PSYPAG; ISSN: 0033-3158
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Direct hippocampal injection of Na UMP (Na-I) [**7545-48-4**] (40 .mu.g) into rats either 30 min before or 1 min after training for acquisition of a brightness discrimination delayed the extinction of the learned reaction. Hippocampal application of I 60 min after training or injection into the frontal cortex 30 min before the onset of training had no effect on the extinction. None of the types of I treatments used affected the acquisition capability. Thus, I may aid **memory** consolidation, possibly thru an action on RNA synthesis and subsequent protein synthesis. The hippocampus appears to be of importance in the **memory** consolidation process.
IT **7545-48-4**
RL: PRP (Properties)
(**memory** enhancement by hippocampal injection of)
RN 7545-48-4 HCAPLUS
CN 5'-Uridylic acid, sodium salt (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



●x Na

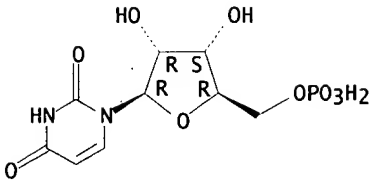
=> d ind 21

L97 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
CC 3-5 (Biochemical Interactions)
ST uridine **memory** consolidation; RNA precursor learning; hippocampus RNA **memory**; UMP **memory** consolidation
IT **Memory, biological**
(RNA precursor enhancement of, after hippocampal injection)
IT Brain
(hippocampus, in **memory** consolidation)
IT Ribonucleic acids
RL: BIOL (Biological study)
(precursors, **memory** enhancement by hippocampal injection of)
IT **7545-48-4**
RL: PRP (Properties)
(**memory** enhancement by hippocampal injection of)

=> d ibib abs hitstr 22 ind

L97 ANSWER 22 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1972:149588 HCAPLUS
DOCUMENT NUMBER: 76:149588
TITLE: Influence of 6-azauridine on facilitation of relearning by precursors of ribonucleic acid
AUTHOR(S): Ott, Tilmann; Matthies, Hansjuergen
CORPORATE SOURCE: Inst. Pharmakol. Toxikol., Med. Akad. Magdeburg, Magdeburg, Ger. Dem. Rep.
SOURCE: Psychopharmacologia (1972), 23(3), 272-8
CODEN: PSYPAG; ISSN: 0033-3158
DOCUMENT TYPE: Journal
LANGUAGE: German
AB Intraventricular injection of orotic acid [65-86-1] or UMP [**58-97-9**] into rats 30 min before training in a conditioned avoidance situation facilitated relearning after a retention of 24 hr. 6-Azauridine (I) [54-25-1], which inhibits the conversion of orotate to UMP, was without effect when given alone, and I did not block the action of UMP when the two were injected together. However, the facilitating effect of orotate was blocked by simultaneous treatment with I. Orotate apparently does not stimulate relearning directly but does so by supplying pyrimidine nucleotide precursors for the increased brain RNA synthesis that occurs during the consolidation of long-term **memory**.
IT **58-97-9**, biological studies
RL: BIOL (Biological study)
(**memory** facilitation by, azauridine effect on)
RN 58-97-9 HCAPLUS
CN 5'-Uridylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

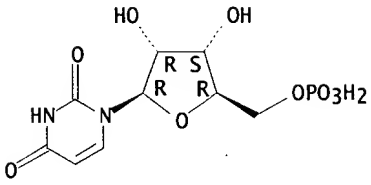


CC 3 (Biochemical Interactions)
ST RNA synthesis brain learning; **memory** brain nucleic acid; orotate brain RNA **memory**; azauridine brain RNA **memory**; UMP brain RNA **memory**
IT Brain, metabolism
(RNA formation by, **memory** in relation to)
IT **Memory, biological**
(RNA precursors facilitation of, azauridine effect on)
IT Ribonucleic acids
RL: FORM (Formation, nonpreparative)
(formation of, by brain, **memory** in relation to)
IT **58-97-9**, biological studies 65-86-1
RL: BIOL (Biological study)
(**memory** facilitation by, azauridine effect on)
IT 54-25-1
RL: PRP (Properties)
(**memory** response to RNA precursors and)

=> d ibib abs hitstr 23 ind

L97 ANSWER 23 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1972:470149 HCAPLUS
DOCUMENT NUMBER: 77:70149
TITLE: Pharmacological influence on the teaching and memorization processes
AUTHOR(S): Matthies, Hansjuergen
CORPORATE SOURCE: Inst. Pharmacol. Toxicol., Med. Acad., Magdeburg, Ger. Dem. Rep.
SOURCE: Farmakologiya i Toksikologiya (Moscow) (1972), 35(3), 259-65
CODEN: FATOAO; ISSN: 0014-8318
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Orotic acid (I) [65-86-1] (100 mg/kg/day) given i.p. to rats for 14 days before or during elaboration of a conditional visual (brightness) discrimination delayed the normal extinction of learned behavior. The length for 50% extinction was 13 days in controls and 215 days in orotic acid-treated animals. This effect of orotic acid was inhibited by azauracil [461-89-2]. UMP [**58-97-9**] and CMP [63-37-6] given i.v. also improved **memory** extension even in the presence of azauracil, indicating that the availability of pyrimidine nucleotides in the brain is a limiting factor for consolidation of long-term **memory**. Trained rats incorporated more UMP into brain RNA and leucine into brain protein than did pseudotrained rats, confirming the participation of intraneuronal regulations in the consolidation of **memory**.
IT **58-97-9**, biological studies
RL: BIOL (Biological study)
(learning and **memory** in response to)
RN 58-97-9 HCAPLUS
CN 5'-Uridylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 1-5 (Pharmacodynamics)
ST orotic acid **memory**; pyrimidine nucleotide **memory**; learning brain protein RNA
IT Brain, metabolism
(RNA formation by, learning and **memory** response to pharmaceutical in relation to)
IT Ribonucleic acids
RL: FORM (Formation, nonpreparative)
(formation of, by brain, learning and **memory** response to pharmaceuticals in relation to)
IT **Learning**
Memory, biological
(pharmaceutical effect on)
IT **58-97-9**, biological studies 63-37-6 65-86-1
RL: BIOL (Biological study)
(learning and **memory** in response to)
IT 461-89-2
RL: BIOL (Biological study)
(learning and **memory** response to orotic acid inhibition by)